Remarks and Arguments

Claims 1-16 and 21 are canceled without prejudice or disclaimer. New claims 22-36 are added. Accordingly, claims 17-20 and 22-36 are pending. Claim 17 is amended to a method of classifying (support at ¶20, line 10) sibling monoclonal antibodies (¶20, lines 3-4); step (b) is amended to recite that each agent is capable of modifying a surface of the immobilized antigen (¶37, lines 14-15). New claim 22 identifies the at least two surfaces as four to nine. Support is found at ¶29, line 3, ¶52, line 1, ¶56, line 13, and the legend of Fig. 2A-B. New claims 23-24 combine original claims 18-20 and are supported in Example 1. New claims 25-29 combine claims 17-20. New claim 30 is drawn to a method of classifying a set of mAb-producing hybridoma clones. Support is found at ¶4, lines 9-12. New claims 31-36 repeat dependent claims 18-20 and 22. No new matter is added by the amendments and new claims, and the Examiner is respectfully requested to enter them.

The Examiner's comments are addressed in the order made.

I. Election/Restriction Requirement

In response to a telephonic Election/Restriction requirement, applicants elected group II (claims 17-21), without traverse. Applicants affirm their election of group II without traverse by telephone on 23 August 2004. Claims 1-16 are herein canceled without prejudice or disclaimer to renewal in a subsequently filed divisional application.

II. Rejections Under the Second Paragraph of § 112.

A. Claim 17 was held to be indefinite for recitation of the phrase ("antigen-specific monoclonal antibodies (mAbs)". In response, claim 17 is amended to recite a method of classifying sibling monoclonal antibodies (mAbs) into functional groups". The term "siblings" is defined at ¶20. Although it is believed that this amendment is fully responsive to the examiner's concerns, applicants are amenable to other language which the examiner should wish to suggest so long as it does not unfairly limit the scope of the claims.

B. Claims 17 was held to be indefinite for recitation of the phrase "is capable of altering the structure of the immobilized antigen." In response, claim 17 has been amended to recite that each agent is capable of modifying a surface of the immobilized antigen. Accordingly, it is believed that this amendment clarifies the metes and bounds of the claim and thus the rejection may now be withdrawn.

C. Claim 17 was held to be indefinite for the term "structure." This rejection is rendered moot by the above amendment removing the term "structure."

D. Claim 17 was rejected as indefinite for recitation of the term "sorting." Although it is believed that claim 17 is not rendered indefinite by this term, claim 17 is amended to replace "sorting" with "classifying". Support for this amendment is found in ¶20. Accordingly, this rejection may now be withdrawn.

E. Claim 1 (believed to be directed to claim 17) was rejected for lack of antecedent basis for the term "the antigen." This rejection is rendered moot by the above amendments to the claim.

F. Claim 21 was held to be indefinite for recitation of specific trademarks/tradenames. The rejection is rendered moot by cancellation of the claim.

III. Rejection Under 35 USC § 103(a).

A. Claim 17 was rejected as obvious over Colyer et al. (WO 00/50902) in view of Pfund et al. (Molecular Immunology, 1990, 27(6):495-502). This rejection is respectfully traversed.

Obviousness is a legal conclusion based on underlying facts of four general types: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any objective indicia of nonobviousness. See Graham v. John Deere Co., 383 U.S. 1, 17-18, 15 L. Ed. 2d 545, 86 S. Ct. 684 (1966); Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1270, 20 USPQ2d 1746, 1750-51 (Fed. Cir. 1991); Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1566-68, 1 USPQ2d 1593, 1594 (Fed. Cir. 1987).

The invention as claimed. Claim 17 is drawn to a method of classifying sibling monoclonal antibodies (mAbs) into functional groups, comprising: (a) immobilizing the antigen onto at least two biosensor surfaces; (b) treating each biosensor surface with a different agent, wherein each agent is capable of modifying a surface of the immobilized antigen; (c) exposing each treated biosensor surface to each mAb; (d) determining a binding profile for each mAb; and(e) classifying the mAbs into functional groups based on the binding profiles, wherein mAbs that exhibit similar binding profiles to each treated sensor surface are classified into the same functional group.

Colyer et al. (WO 00/50902). Colyer et al. describe a high throughput assay for analyzing a sample in which two polypeptides capable of associating are provided. The first polypeptide is immobilized on a solid support, and the polypeptides allowed to associate such

that a detectable signal is induced. The polypeptides are contacted with an agent, such as an enzyme, and the signal detected and compared to the first (reference) signal. In one variation, the immobilized first polypeptide is treated with a sample that is suspected of containing a modifying agent. Following treatment of the first polypeptide with the sample, the first polypeptide is exposed to the second polypeptide and the surface is observed to determine the effect that exposure to the sample had on the binding of the first and second polypeptide. The method described by Colyer et al. assays for protein modifying enzymes present in a sample by the effect on the interaction of the polypeptide pair.

Colyer et al. do not describe or suggest (1) a method of classifying sibling monoclonal antibodies into functional groups; (2) immobilizing the antigen onto at least two biosensor surfaces; (3) treating each biosensor surface with a different modifying agent; and (4) classifying the mAbs into functional groups based on the binding profiles, wherein mAbs that exhibit similar binding profiles to each treated sensor surface are classified into the same functional group.

Pfund et al. (Molecular Immunology, 1990, 27(6):495-502). Pfund et al. describes a conformation-sensitive immunoassay (CSI) for identifying conformation-sensitive antibodies. (page 495, col. 2, last paragraph). The Pfund et al. method covalently binds antigen to a membrane. Membrane bound antigen is incubated under physiological or denaturing conditions, and then exposed to mAbs. Antibodies are identified that demonstrate significant binding to native protein only are most likely binding to residues that are distant in sequence but brought into close proximity in the native 3-D structure (e.g., anti-sSt-7, page 500, col. 2, last paragraph). Antibodies that demonstrate significant binding to denatured antigen only indicate binding to a contiguous epitope that is buried within the native structure (e.g., anti-bSt-16, page 501, col. 1, first full paragraph). Antibodies that exhibit strong binding to both native and denatured antigen indicate binding to surface exposed determinants.

Pfund et al. do not disclose or suggest (1) immobilizing the antigen onto at least two biosensor surfaces; (2) treating each biosensor surface with different modifying agents.

The analysis under § 103(a). Applicants respectfully submit that the cited prior art references, either taken together or alone, do not render the claimed invention obvious.

As the analysis above reveals, both references fail to disclose or suggest a method which can achieve that of the instant invention – that is, to separate into groups antibodies specific to the same antigen on the basis of their binding profile to the same antigen modified by at least two different agents. The instant claims require at least two biosensor surfaces with the same attached antigen. In contrast, Colyer et al. disclose that an unknown sample potentially

containing a modifying agent is exposed to two different immobilized polypeptides (see, for example, Fig. 17 of Colyer et al.). The instant claims require that each surface containing the same immobilized antigen be treated with different but known modifying agents. In contrast, Colyer et al. teaches treating the immobilized polypeptide with a single sample potentially containing an unknown modifying agent.

It is not clear to applicants how Pfund et al. can be combined with Colyer et al. since Pfund et al. teach away from the use of two (or more) distinct assay systems in favor of a single method for testing antibody reactivities. Nonetheless, if for the sake of argument the references are combinable, which applicant does not concede, the combination would still not produce the claimed method since neither reference disclose or suggest (1) immobilizing the antigen onto at least two biosensor surfaces; (2) treating each biosensor surface with different modifying agents.

The examiner is respectfully reminded that a determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination."). The analysis above establishes that the cited prior art, alone or in combination, fails to teach or suggest the method of the invention. Indeed, the problem addressed by the prior art and the solution achieved are quite different from that of the instant invention. Even if the method of Colyer et al. is modified with "conformation-sensitive" mAb anti-bSt-1 through anti-bSt-4, anti-bSt-7, and anti-bSt-16, as stated by the examiner at page 9 of the Office action, one would not obtain the instant method because the instant method is not distinguishing antibodies based on binding profiles to native and denatured antigen. In contrast to the prior art methods, the present invention groups antibodies on the basis of their binding profiles to at least two modified versions of the same antigen. Accordingly, in light of the above remarks, it is respectfully requested that this rejection be

withdrawn.

B. Claim 20 was rejected as obvious over Colyer et al. (WO 00/50902) in view of Pfund et al. (Molecular Immunology, 1990, 27(6):495-502). This rejection is respectfully traversed.

The invention as claimed. Claim 20 is drawn to the method of claim 17 (summarized above) wherein the agent is selected from the group consisting of Tris (2-carboxyethyl) phosphine hydrochloride (TCEP•HCl), N-ethyl-N'-(dimethylaminopropyl) carbodiimide (EDC), iodoacetamide, hydrazine, p-hydroxyphenylglyoxal (HPG), hydrogen peroxide, N-bromosuccinimide, N-acetylimidazole, tetranitromethane, arsanilic acid, dansyl chloride, glutaraldehyde, ninhydrin, and diethylpyrocarbonate (DEPC).

Lin et al. (Journal of Food Science 1976, 41(5):1056-1060. Lin et al. discloses chemical modification of a collagen membrane by glutaraldehyde to cross-link the collagen membrane in order to determine the effect of the chemical modification on the enzyme-binding capacity of the collagen membrane.

Lin et al. does not disclose, teach, or suggest (1) immobilizing an antigen onto at least two biosensor surfaces, (2) the effect of chemical modification of antigen on the binding between antigen and its monoclonal antibodies, (3) determining the binding profile of mAbs to its antigen, or (4) classifying the mAbs into functional groups based on the binding profile of the mAbs to each modified antigen.

Analysis under § 103(a). The above remarks are fully applicable to this rejection and are herein incorporated by reference. Applicants submit that the combined references do not teach or suggest the instant invention. Nothing in the cited references yields a method which allows antibodies to the same antigen to be grouped on the basis of their binding profiles to at least two modified versions of the same antigen. Accordingly, in light of the above remarks, it is respectfully requested that this rejection be withdrawn.

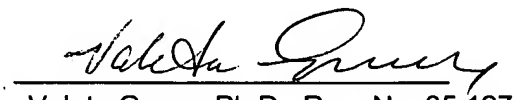
Conclusion

It is believed that this document is fully responsive to the matters raised in the Office action dated 24 September 2004. In light of the above amendments and remarks, it is believed that the claims are now in condition for allowance, and such action is respectfully urged.

Fees

Applicants contend that no fee is necessary in connection with the filing of this response. However, if any fee is deemed to be necessary, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 18-0650.

Respectfully submitted,



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